

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

PTO/SB/08A (08-03)

Approved for use through 07/31/2006. OMB 0651-0031
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Substitute for form 1449A-PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet 1 of 7

Complete if Known

Application Number	10/681,418
Filing Date	October 7, 2003
First Named Inventor	H. Michael SHEPARD
Art Unit	Lawrence E. Crane
Examiner Name	1623
Attorney Docket Number	NB 2008.01

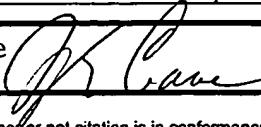
U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Document Number Number – Kind Code ² (if known)	Publication Date MM-DD-YY	Name of Patentee or Application of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
JKC	1	US-3,852,266	12-03-74	Kiyanagi et al.	
JKC	2	US-4,247,544	01-27-81	Bergstrom, et al.	
	3	US-4,267,171	04-12-81	Bergstrom, et al.	
	4	US-4,542,210	09-17-85	Sakata et al.	
	5	US-4,668,777	05-26-87	Caruthers et al.	
	6	US-4,816,570	03-28-89	Farquhar	
	7	US-4,948,882	08-14-90	Ruth	
	8	US-4,963,263	10-16-90	Kauver	
JKC	9	US-4,963,533	10-16-90	De Clercq et al.	
JKC	10	US-4975,278	12-04-90	Senter et al.	

** Duplicate: see PTO-892 for citation.

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Foreign Patent Document Country Code ³ – Number ⁴ – Kind Code ⁵ (if known)	Publication Date MM-DD-YY	Name of Patentee or Application of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶
JKC	11	DE 32 29 169 A1	02-09-84	De Clercq et al.		
JKC	12	EP 0 311 107 A2	04-12-89	Stichting REGA VZW		
JKC	13	EP 0 311 108A2	04-12-89	Stichting REGA VZW		
JKC	14	EP 0 316 592	05-24-89	Stichting REGA VZW		
JKC	15	GB 982 776	02-10-65	The Wellcome Foundation		
JKC	16	RO 88451	01-30-86	Antibiotics Enterprise, Iasi		X
JKC	17	WO 89/05817	06-29-89	Nucleic Acid Research Institute		
JKC	18	WO 90/03978	04-19-90	Stichting REGA VZW		
JKC	19	WO 91/17424	11-14-91	Vical, Inc.		

Examiner's Signature	L. E. Crane 	Date Considered	02/22/2005
----------------------	---	-----------------	------------

* EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. ¹ Applicant's unique citation designation number (optional). ² See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached.

The collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2.0 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing this form, call 1-800-PTO-9199 and select option 2.

10/681,418 - PTO-1449 #1

COPY FOR [] Fiduciary Applicant

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form1449A-PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet

2

of

7

Complete if Known

Application Number	10/681,418
Filing Date	October 7, 2003
First Named Inventor	H. Michael SHEPARD
Art Unit	Lawrence E. Crane
Examiner Name	1623

Attorney Docket Number

NB 2008.01

U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Document Number	Publication Date MM-DD-YY	Name of Patentee or Application of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number – Kind Code ² (if known)			
**	20	US-5,070,982	12-03-91	Murdeek, et al. (I)	
**	21	US-5,077,262	12-31-91	Murdeek, et al. (II)	
**	22	US-5,077,263	12-31-91	Murdeek, et al. (III)	
**	23	US-5,085,983	02-04-92	Scanlon	
**	24	US-5,116,822	05-26-92	De Clercq et al.	
**	25	US-5,116,827	05-26-92	Murdock, et al. (IV)	
**	26	US-5,133,866	07-28-92	Kauver	
**	27	US-5,137,724	08-11-92	Balzarini et al.	
**	28	US-5,212,161	03-18-93	Morniere et al.	
**	29	US-5,212,201	03-18-93	Murdeek, et al. (V)	

** Duplicate: see PTO-892 for citation.

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YY	Name of Patentee or Application of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶
		Country Code ³ – Number ⁴ – Kind Code ⁵ (if known)				
**	30	WO 92/19767	11-12-92	Terrapin Technologies, Inc.		
**	31	WO 93/06120	04-01-93	University of Rochester		
**	32	WO 94/03467	02-17-94	Institute of Organic Chemistry & Biochemistry of the Academy of Sciences of the Czech Republic, et al.		
**	33	WO 94/22483	10-13-94	Kozak, Alexander		

Examiner's Signature	L. E. Crane	Date Considered	02/22/2005
----------------------	-------------	-----------------	------------

* EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. ¹ Applicant's unique citation designation number (optional). ² See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 801.04. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached.

The collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2.0 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing this form, call 1-800-PTO-9199 and select option 2.

Substitute for form 1449A-PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet

3

of

7

Complete if Known

Application Number	10/681,418
Filing Date	October 7, 2003
First Named Inventor	H. Michael SHEPARD
Art Unit	Lawrence E. Crane
Examiner Name	1623

Attorney Docket Number

NB 2008.01

U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Document Number	Publication Date MM-DD-YY	Name of Patentee or Application of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number – Kind Code ² (if known)			
<i>He</i>	34	US-5,217,869	06-08-93	Kauver	
	35	US-5,233,031	08-03-92	Borch et al.	
	36	US-5,264,618	11-23-93	Felgner et al.	
	37	US-5,300,425	04-05-94	Kauver	
	38	US-5,338,659	08-16-94	Kauver, et al.	
	39	US-5,430,148	07-04-95	Webber, et al.	
<i>He</i>	40	US-5,433,955	07-18-95	Brededorst et al.	
xx	41	US-5,457,187	10-10-95	Gmeiner et al.	
<i>He</i>	42	US-5,459,127	10-17-95	Felgner et al.	
<i>He</i>	43	US-5,516,631	05-14-96	Frisch	

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YY	Name of Patentee or Application of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁴
		Country Code ³ – Number ⁴ – Kind Code ⁵ (if known)				
<i>He</i>	44	WO 95/01806	01-19-95	Kondratyev, A.		
xx	45	WO 95/08556	03-30-95	Amercham International, Inc.		
<i>He</i>	46	WO 95/09865	04-13-95	Terrapin Technologies, Inc.		
<i>He</i>	47	WO 95/12678	05-11-95	Connors, T. et al.		
xx	48	WO 96/03151	02-08-96	Springer et al.		
<i>He</i>	49	WO 96/07413	04-04-96	University of Georgia Research Foundation & Yale University		

Examiner's Signature

L. E. Crane

Date Considered

02/22/2005

* EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. ¹ Applicant's unique citation designation number (optional). ² See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached.

The collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2.0 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

** Duplicate: see PTO-892 for citation.
If you need assistance in completing this form, call 1-800-PTO-9199 and select option 2.

10/681,418 - PTO-1449 #1

COPY FOR [] File [] Applicant

Substitute for form1449A-PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet

4

of

7

Complete if Known

Application Number	10/681,418
Filing Date	October 7, 2003
First Named Inventor	H. Michael SHEPARD
Art Unit	Lawrence E. Crane
Examiner Name	1623

Attorney Docket Number

NB 2008.01

U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Document Number	Publication Date MM-DD-YY	Name of Patentee or Application of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number – Kind Code ² (if known)			
	50	US-5,521,161	05-28-96	Malley et al.	
	51	US-5,527,900	06-18-96	Balzarini et al.	
	52	US-5,596,018	01-21-97	Baba et al.	
	53	US-5,616,564	04-01-97	Rapaport	
	54	US-5,627,165	05-06-97	Glazier	
	55	US-5,645,988	07-08-97	Vande Woude et al.	
	56	US-5,663,321	09-02-97	Gmeiner et al.	
	57	US-5,733,896	03-31-98	Holý et al.	
	58	US-5,798,340	08-25-98	Bischofberger et al.	
	59	US-5,968,910	10-19-99	Balzarini	

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YY	Name of Patentee or Application of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶
		Country Code ³ – Number ⁴ – Kind Code ⁵ (if known)				
	60	WO 96/10030	04-04-96	Icis Pharmaceuticals, Inc.		
	61	WO 96/23506	08-08-96	Fraunhofer Society for the Promotion of Applied Research E.V.		X
	62	WO 96/29336	09-26-96	Medical Research Council, University College Cardiff Consultants, Inc. Rega Foundation		

Examiner's Signature	L. E. Crane	Date Considered	02/22/2005
----------------------	-------------	-----------------	------------

** Duplicate: see PTO-892 for citation.

* EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. ¹ Applicant's unique citation designation number (optional). ² See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 801.04. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached.

The collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2.0 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing this form, call 1-800-PTO-9199 and select option 2.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A-PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet 5 of 7 Attorney Docket Number NB 2008.01

Complete if Known

Application Number	10/681,418
Filing Date	October 7, 2003
First Named Inventor	H. Michael SHEPARD
Art Unit	Lawrence E. Crane
Examiner Name	1623

U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Document Number	Publication Date MM-DD-YY	Name of Patentee or Application of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number – Kind Code ² (if known)			
JK	63	US-5,981,507	11-09-99	Josephson et al.	
JK	64	US-6,057,305	05-02-00	Holy et al.	
JK	65	US-6,245,750	06-12-01	Shepard	
**	66	US-6,330,161	02-16-02	Shepard et al.	
**	67	US-6,406,553	12-17-02	Shepard	
**	68	US-2001/034440	10-25-01	Shepard et al.	
**	69	US-2002/0147175	10-10-02	Shepard et al.	
**	70	US-2002/0151519	10-17-02	Shepard et al.	

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YY	Name of Patentee or Application of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶
		Country Code ³ – Number ⁴ – Kind Code ⁵ (if known)				
JK	71	WO 96/33168	10-24-96	Kumai Chemical Industry Co Ltd et al.		
JK	72	WO 96/40088	12-19-96	Hostettler, Karl Y.		
JK	73	WO 96/40708	12-10-96	La Jolla Pharmaceuticals, Inc.		
JK	74	WO 96/40739	12-19-96	Terrapin Technologies, Inc.		
JK	75	WO 97/25342	07-17-97	Terrapin Technologies, Inc.		
**	76	WO 97/28170	08-07-97	Fick, James & Israel, Mark		

Examiner's Signature	L. E. Crane	Date Considered	02/22/2005
----------------------	-------------	-----------------	------------

** Duplicate: see PTO-899 for citation.

* EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. ¹ Applicant's unique citation designation number (optional). ² See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached.

The collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2.0 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing this form, call 1-800-PTO-9199 and select option 2.

10/681,418 PTO-1449 #1

COPY FOR [] File [] Applicant

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A-PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet 6 of 7

Complete if Known

Application Number	10/681,418
Filing Date	October 7, 2003
First Named Inventor	H. Michael SHEPARD
Art Unit	Lawrence E. Crane
Examiner Name	1623
Attorney Docket Number	NB 2008.01

U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Document Number	Publication Date MM-DD-YY	Name of Patentee or Application of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number – Kind Code ² (if known)			

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YY	Name of Patentee or Application of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶
		Country Code ³ – Number ⁴ – Kind Code ⁵ (if known)				
<i>gfe</i>	77	WO 97/49717	12-31-97	Balzarini et al.		
<i>gfe</i>	78	WO 98/49177	11-05-98	University College Cardiff Consultants Limited		
<i>Ree</i>	79	WO 99/06072	02-11-99	Boehringer Mannheim Corp.		
**	80	WO 99/08110	02-18-99	NewBiotics, Inc.		
**	81	WO 99/20741	04-20-99	Geron Corporation		
<i>Ree</i>	82	WO 99/23104	05-14-99	The Government of the United States of America represented by The Secretary of Health & Human Services		
**	83	WO 99/27763	07-20-99	NewBiotics, Inc.		

Examiner's Signature	L. E. Crane 	Date Considered	02/22/2005
----------------------	---	-----------------	------------

** Duplicate: See pto-892 for citation.

* EXAMINER: Initial if reference considered; whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. ¹ Applicant's unique citation designation number (optional). ² See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached.

The collection of information is required by 37 CFR 1.87 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2.0 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing this form, call 1-800-PTO-9199 and select option 2.

10/681,418 - TPO-1449 #1

COPY FOR [] File [] Applicant

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form1449A-PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet 7 of 7

Complete if Known

Application Number	10/681,418
Filing Date	October 7, 2003
First Named Inventor	H. Michael SHEPARD
Art Unit	Lawrence E. Crane
Examiner Name	1623

Attorney Docket Number

NB 2008.01

U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Document Number	Publication Date MM-DD-YY	Name of Patentee or Application of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number – Kind Code ² (if known)			

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YY	Name of Patentee or Application of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶
		Country Code ³ – Number ⁴ – Kind Code ⁵ (if known)				
	84	WO 00/18755	04-06-00	University College Cardiff Consultants Limited and Rega Foundation		
	85	WO 00/33888	06-15-00	Dubois, V. et al.		
	86	WO 01/07088	02-01-01	NewBiotics, Inc.		
	87	WO 01/83501	11-08-01	University College Cardiff Consultants Limited and Rega Foundation		
	88	WO 01/85749	11-15-01	University College Cardiff Consultants Limited and Rega Foundation		

Examiner's Signature

L. E. Crane

Date Considered

02/22/2005

* EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. ¹ Applicant's unique citation designation number (optional). ² See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached.

The collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2.0 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing this form, call 1-800-PTO-9199 and select option 2.

10/681,418 - PTO=1449 #1

COPY FOR [] File Applicant

Substitute for form 1449B PTO

INFORMATION DISCLOSURE
STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet 1 of 19

Complete if Known

Application Number	10/681,418
Filing Date	October 7, 2003
First Named Inventor	H. Michael SHEPARD
Art Unit	Lawrence E. Crane
Examiner Name	1623

Attorney Docket Number NB 2008.01

NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher city and/or country where published	T ²
<i>JMC</i>	1 !	ABRAHAM et al. "Synthesis and biological activity of aromatic amino acid phosphoramidates of 5-fluoro-2'-deoxyuridine and 1-β-arabinofuranosylcytosine: Evidence of phosphoramidase activity" <i>J. Med. Chem.</i> (1996) 39:4569-4575	
	2 !	AKDAS et al. "Glutathione S-transferase and multidrug-resistant phenotype in transitional cell carcinoma of the bladder" <i>Eur. Urol.</i> (1996) 29(4):483-486	
	3	ALMASAN et al. "Deficiency of retinoblastoma protein leads to inappropriate S-phase entry, activation of E2F-responsive genes, and apoptosis" <i>PNAS, USA</i> (June 1995) 92:5436-5440	
	4 !	ALMASAN et al. "Genetic instability as a consequence of inappropriate entry into and progression through S-phase" <i>Cancer Metast. Rev.</i> (1995) 14:59-73	
	5	ANGLADA et al. "N,N-cyclization of carbodiimides with 2-(bromomethyl)acrylic acid. A direct entry to the system 5-methylene-6H-pyrimidine-2,4-dione, A new class of thymine analogues" <i>J. Heterocyclic Chem.</i> (July-Aug. 1996) 33:1259-1270	
	6 !	ANTELMAN et al. "Inhibition of tumor cell proliferation in vitro and in vivo by exogenous p110 ^{RB} , the retinoblastoma tumor suppressor protein" <i>Oncogene</i> (1995) 10:697-704	
	7 !	ASAKURA and ROBINS, "Cerium(IV) catalyzed iodination at C5 of uracil nucleosides" <i>Tetrahedron Lett.</i> (1988) 29(23):2855-2858	
	8 !	ASAKURA et al. "Cerium(IV)-mediated halogenation at C-5 of uracil derivatives" <i>J. Org. Chem.</i> (1990) 55:4928-4933	
	9	ASCHELE et al. "Immunohistochemical quantitation of thymidylate synthase expression in colorectal cancer metastases predicts for clinical outcome to fluorouracil-based chemotherapy" <i>J. Clin. Oncol.</i> (June 1999) 17(6):1760-1770	
	10 !	BAGSHAWE, K.D. "Antibody-directed enzyme prodrug therapy: A review", <i>Drug Develop. Res.</i> (1995) 34(2):220-230	
	11 !	BAJETTA et al. "A pilot safety study of capecitabine, a new oral fluoropyrimidine, in patients with advanced neoplastic disease" <i>Tumori</i> (1996) 82:450-452	
	12 !	BALZARINI et al. "Incorporation of 5-substituted pyrimidine nucleoside analogues into DNA of a thymidylate synthetase-deficient murine FM3A carcinoma cell line" <i>Meth. Find. Exp. Clin. Pharmacol.</i> (1985) 7(1):19-28	
<i>JMC</i>	13 !	BALZARINI et al. "The cytostatic activity of 5-(1-azidovinyl)-2'-deoxyuridine (AzVDU) against herpes simplex virus thymidine kinase gene-transfected FM3A cells is due to inhibition of thymidylate synthase and enhanced by UV light ($\lambda = 254$ nm) exposure" <i>FEBS Lett.</i> (1995) 373:41-44	

Examiner's Signature	L. EQ Crane	Date Considered	03/08/2005
----------------------	-------------	-----------------	------------

! Month of publication data not available on copy supplied.

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Applicant's unique citation designation number (optional). ² Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.98. This information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 120 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing this form, call 1-800-PTO-9199 and select option 2.

10/681,418 - PTO-1449 #2

COPY FOR [] File Applicant

Substitute for form 1449B-PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet 2 of 19

Complete if Known

Application Number	10/681,418
Filing Date	October 7, 2003
First Named Inventor	H. Michael SHEPARD
Art Unit	Lawrence E. Crane
Examiner Name	1623
Attorney Docket Number	NB 2008.01

NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher city and/or country where published	T ²
<i>Hec</i>	14	BALZARINI et al. "Mechanism of anti-HIV action of masked alaninyl d4T-MP derivatives" <i>PNAS USA</i> (July 1996) 93:7295-7299	
	15 !	BANERJEE et al. "Molecular mechanisms of resistance to antifolates, a review" <i>Acta Biochim. Pol.</i> (1995) 42(4):457-464	
	16	BANERJEE et al. "Role of E2F-1 in chemosensitivity" <i>Cancer Res.</i> (Oct. 1, 1998) 58:4292-4296	
	17 !	BARBATO et al. "Synthesis of bridged pyrimidine nucleosides and triazo [4, 3-c] pyrimidine nucleoside analogues" <i>Nucleos. Nucleot.</i> (1989) 8(4):515-528	
	18 !	BARBOUR et al. "A naturally occurring tyrosine to histidine replacement at residue 33 of human thymidylate synthase confers resistance to 5-fluoro-2'-deoxyuridine in mammalian and bacterial cells" <i>Mol. Pharmacol.</i> (1992) 42:242-248	
	19 !	BARR et al. "Reaction of 5-ethynyl-2'-deoxyuridylate with thiols and thymidylate synthetase" <i>Biochemistry</i> (1983) 22:1696-1703	
	20 !	BARRETT "Trapping of the C5 methylene intermediate in thymidylate synthase" <i>J. Am. Chem. Soc.</i> (1998) 120:449-450	
<i>Hec</i>	21 !	BENZARIA et al. "Synthesis, <i>in vitro</i> antiviral evaluation, and stability studies of bis(S-acyl-2-thioethyl) ester derivatives of 9-[2-(phosphonomethoxy)ethyl]adenine (PMEA) as potential PMEA prodrugs with improved oral bioavailability" <i>J. Med. Chem.</i> (1996) 39:4958-4965	
<i>Hec</i>	22	BERGSTROM et al. "Synthesis of (E)-5-(3,3,3-trifluoro-1-propenyl)-2'-deoxyuridine and related analogues: Potent and unusually selective antiviral activity of (E)-5-(3,3,3-trifluoro-1-propenyl)-2'-deoxyuridine against herpes simplex virus type 1" <i>J. Med. Chem.</i> (1984) 27:279-284	
<i>Hec</i>	23 !	BERTINO et al. "Resistance mechanisms to methotrexate in tumors" <i>Stem Cells</i> (1996) 14:5-9	
<i>Hec</i>	24	BIGGE et al. "Palladium-catalyzed coupling reactions of uracil nucleosides and nucleotides" <i>J. Amer. Chem. Soc.</i> (Mar. 12, 1980) 102(6):2033-2038	
<i>Hec</i>	25 !	BUDAVARI (July 1996) (Ed.), <i>The Merck Index</i> , 12 th Edition, Doxifluridine, page 3493	
	26 !	BUDAVARI (July 1996) (Ed.), <i>The Merck Index</i> , 12 th Edition, Floxuridine, page 4148	
	27 !	BUDAVARI (July 1996) (Ed.), <i>The Merck Index</i> , 12 th Edition, Idoxuridine, page 4934	
	28	CALLAHAN et al. "Rhenium-188 for therapeutic applications from an alumina-based tungsten-188/rhenium-188 radionuclide generator" <i>Nuc-Compact</i> (Jan 1989) 20:3-6	
	29 !	CARRERAS and SANTI "The catalytic mechanism and structure of thymidylate synthase" <i>Annu. Rev. Biochem.</i> (1995) 64:721-762	
<i>Hec</i>	30	CARTER et al. "Humanization of an anti-p185 ^{HER2} antibody for human cancer therapy" <i>PNAS USA</i> (May 1992) 89:4285-4289	

Examiner's Signature	L. E. Crane <i>Hec Crane</i>	Date Considered	03/08/2005
----------------------	------------------------------	-----------------	------------

! Month of publication date not available on copy supplied.

* EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 809. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Applicant's unique citation designation number (optional). ² Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.88. This information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 120 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

** Duplicate: see PTO-892 for citation.

If you need assistance in completing this form, call 1-800-PTO-9199 and select option 2.

Substitute for form 1449B-PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet 3 of 19

Complete if Known

Application Number	10/681,418
Filing Date	October 7, 2003
First Named Inventor	H. Michael SHEPARD
Art Unit	Lawrence E. Crane
Examiner Name	1623

Attorney Docket Number

NB 2008.01

NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher city and/or country where published	T ²
<i>Lee</i>	31 !	CASS et al. "Recent advances in the molecular biology of nucleoside transporters of mammalian cells" <i>Biochem. Cell Biol.</i> (1998) 76(5):761-770	
<i>Lee</i>	32	CATUCCI et al. "Development and significance of the HIV-1 reverse transcriptase M184V mutation during combination therapy with lamivudine, zidovudine, and protease inhibitors" <i>J. Acquir. Immune Defic. Syndr.</i> (July 1999) 21(3):203-208	
<i>Lee</i>	33 !	CHAUDHURI and KOOL "Very high affinity DNA recognition by bicyclic and cross-linked oligonucleotides" <i>J. Am. Chem. Soc.</i> (1995) 117:10434-10442	
<i>Lee</i>	34	CHEN et al. "Sensitization of human breast cancer cells to cyclophosphamide and ifosfamide by transfer of a liver cytochrome P450 gene" <i>Cancer Res.</i> (Mar. 15, 1996) 56:1331-1340	
**	35	GHO and JOHNSON "(E)-5-(3-oxopropen-1-yl)-2'-deoxyuridine and (E)-5-(3-oxopropen-1-yl)-2',3'-dideoxyuridine; New antiviral agents: Synthesis and biological activity" <i>Tetrahedron Lett.</i> (1994) 35(8):1149-1152	
<i>Lee</i>	36 !	CLARKE "Animal models of breast cancer: Their diversity and role in biomedical research" <i>Breast Cancer Res. Tr.</i> (1996) 39:1-6	
<i>Lee</i>	37	COBLEIGH et al. "Multinational study of the efficacy and safety of humanized anti-HER2 monoclonal antibody in women who have HER2-overexpressing metastatic breast cancer that has progressed after chemotherapy for metastatic disease" <i>J. Clin. Oncol.</i> (Sept. 1999) 17(9):2639-2648	
<i>Lee</i>	38 !	CODERRE et al. "Mechanism of action of 2',5-difluoro-1-arabinosyluracil" <i>J. Med. Chem.</i> (1983) 26(8):1149-1152	
<i>Lee</i>	39 !	CONNORS and KNOX "Prodrugs in cancer chemotherapy" <i>Stem Cells</i> (1995) 13:501-511	
<i>Lee</i>	40 !	COPUR et al. "Thymidylate synthase gene amplification in human colon cancer cell lines resistant to 5-fluorouracil" <i>Biochem. Pharmacol.</i> (1995) 49(10):1419-1426	
<i>Lee</i>	41 !	COSTI et al. "Phthalein derivatives as a new tool for selectivity in thymidylate synthase inhibition" <i>J. Med. Chem.</i> (1999) 42(12):2112-2124	
**	42	CRIEP "Synthesis of 5-alkenyl-2'-deoxyuridines via organostannanes" <i>Synth. Commun.</i> (1989) 19(11 & 12):2117-2123	
<i>Lee</i>	43 !	CRUICKSHANK et al. "Oligonucleotide labelling: A concise synthesis of a modified thymidine phosphoramidite" <i>Tetrahedron Lett.</i> (1988) 29(41):5221-5224	
<i>Lee</i>	44	DALE et al. "The synthesis and enzymatic polymerization of nucleotides containing mercury: Potential tools for nucleic acid sequencing and structural analysis" <i>PNAS USA</i> (August 1973) 70(8):2238-2242	

Examiner's Signature

L. E. Crane

Date Considered

03/08/2005

! Month of publication data not available on copy supplied.

* EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Applicant's unique citation designation number (optional). ² Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.98. This information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 120 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

** DUPLICATE: see pto-892 for citation.

If you need assistance in completing this form, call 1-800-PTO-9199 and select option 2.

Substitute for form 1449B-PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet 4 of 19

Complete if Known

Application Number	10/681,418
Filing Date	October 7, 2003
First Named Inventor	H. Michael SHEPARD
Art Unit	Lawrence E. Crane
Examiner Name	1623

Attorney Docket Number NB 2008.01

NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher city and/or country where published	T ²
<i>Lee</i>	45	DeCLERCQ et al. "Antiviral Activity of Novel Deoxyuridine Derivatives" <u>Current Chemotherapy: Proceedings of the International Congress of Chemotherapy</u> published in <u>Virology</u> (Sept. 18, 1978) 1:352-354	
	46 !	DeCLERCQ et al. "Nucleic acid related compounds. 40. Synthesis and biological activities of 5-alkynyluracil nucleosides" <u>J. Med. Chem.</u> (1983) 26:661-666	
	47 !	DeCLERCQ "Antiviral Activity Spectrum and Target of Action of Different Classes of Nucleoside Analogues" <u>Nucleos. Nucleot.</u> (1994) 13(6&7):1271-1295	
	48	DICKER et al. "Methotrexate resistance in an <i>in vivo</i> mouse tumor due to a non-active-site dihydrofolate reductase mutation" <u>PNAS USA</u> (Dec. 1993) 90:11797-11801	
	49	DIRVIN et al. "The role of human glutathione S-transferase isoenzymes in the formation of glutathione conjugates of the alkylating cytostatic drug thiotepa" <u>Cancer Res.</u> (April 15, 1995) 55:1701-1706	
	50 !	DORR and von HOFF "PALA" In: <u>Cancer Chemotherapy Handbook</u> , 2nd Edition, Appleton & Lange, Norwalk, Connecticut (1994) pp. 768-773	
	51 !	DUNN et al. "Solution of the conformation and alignment tensors for the binding of trimethoprim and its analogs to dihydrofolate reductase: 3D-quantitative structure-activity relationship study using molecular shape analysis, 3-way partial least-squares regression, and 3-way factor analysis" <u>J. Med. Chem.</u> (1996) 39:4825-4832	
	52 !	DYER et al. "Nucleic Acids Chemistry: Improved and new synthetic procedures, methods, and techniques" Townsend, L. B. & Tipson, R. S., eds. (Wiley-Interscience, New York, NY) (1991) 4:79-83	
	53	EDLER et al. "Immunohistochemically detected thymidylate synthase in colorectal cancer: An independent prognostic factor of survival" <u>Clinical Cancer Research</u> (Feb. 2000) 6:488-492	
	54 !	FAN and BERTINO "Functional roles of E2F in cell cycle regulation" <u>Oncogene</u> (1997) 14:1191-1200	
	55 !	FARQUHAR et al. "Synthesis and antitumor evaluation of bis[(pivaloyloxy)methyl] 2'-deoxy-5-fluorouridine 5'-monophosphate (FdUMP): A strategy to introduce nucleotides into cells" <u>J. Med. Chem.</u> (1994) 37:3902-3909	
	56 !	FARQUHAR et al. "5'-[4-pivaloyloxy]-1,3,2-dioxaphosphorinan-2-yl]-2'-deoxy-5-fluorouridine: A membrane-permeating prodrug of 5-fluoro-2'-deoxyuridyllic acid (FdUMP)" <u>J. Med. Chem.</u> (1995) 38:488-495	
<i>Lee</i>	57 !	FARROW et al. "Synthesis and biological properties of novel phosphotriesters: A new approach to the introduction of biologically active nucleotides into cells" <u>J. Med. Chem.</u> (1990) 33(5):1400-1406	

Examiner's Signature	L. E. Crane	Date Considered	03/08/2005
----------------------	-------------	-----------------	------------

! Month of publication data not available on copy supplied.

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Applicant's unique citation designation number (optional). ² Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.88. This information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 120 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing this form, call 1-800-PTO-9199 and select option 2.

10/681,418, - PTO-1449 #2

COPY FOR [] File Applicant

Substitute for form 1449B-PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet

5

of

19

Complete if Known

Application Number	10/681,418
Filing Date	October 7, 2003
First Named Inventor	H. Michael SHEPARD
Art Unit	Lawrence E. Crane
Examiner Name	1623

Attorney Docket Number

NB 2008.01

NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher city and/or country where published	T ²
<i>He</i>	58 !	FELMINGHAM and WASHINGTON "Trends in the antimicrobial susceptibility of bacterial respiratory tract pathogens – findings of the Alexander Project 1992-1996" <i>J. Chemotherapy</i> (1999) 11(Suppl 1):5-21	
	59 !	FREED et al. "Evidence for acyloxymethyl esters of pyrimidine 5'-deoxyribonucleotides as extracellular sources of active 5'-deoxyribonucleotides in cultured cells" <i>Biochem. Pharmacol.</i> (1989) 38(19):3193-3198	
<i>He</i>	60 !	FREEMANTLE et al. "Molecular characterisation of two cell lines selected for resistance to the folate-based thymidylate synthase inhibitor, ZD1694" <i>Brit. J. Cancer</i> (1995) 71:925-930	
<i>xx</i>	61	FRIES et al. "Synthesis and biological evaluation of 5-fluoro-2'-deoxyuridine phosphoramidate analogs" <i>J. Med. Chem.</i> (1995) 38(14):2672-2680	
<i>He</i>	62 !	FUNK "Cancer cell cycle control" <i>Anticancer Research</i> (1999) 19:4772-4780	
	63 !	GOLDSTEIN and BROWN "Genetic aspects of disease" In: <i>Harrison's Principles of Internal Medicine</i> , 12th Edition, McGraw-Hill, Inc., New York, NY (1991) pp. 21-76	
	64 !	GOODWIN et al. "Incorporation of alkylthiol chains at C-5 of deoxyuridine" <i>Tetrahedron Lett.</i> (1993) 34(35):5549-5552	
	65 !	GOTTESMANN et al. "Genetic analysis of the multidrug transporter" <i>Annu. Rev. Genet.</i> (1995) 29:607-649	
<i>He</i>	66 !	GRAHAM et al. "DNA duplexes stabilized by modified monomer residues: Synthesis and stability" <i>J. Chem. Soc. Perkin Trans.</i> (1998) 1:1131-1138	
<i>xx</i>	67	GRIENGL et al. "Phosphonoformal and phosphonacetate derivatives of 5-substituted 2'-deoxyuridines: Synthesis and antiviral activity" <i>J. Med. Chem.</i> (1988) 31(9):1831-1839	
<i>xx</i>	68	HOBBS, Jr. "Palladium-catalyzed synthesis of alkynylamino nucleosides. A universal linker for nucleic acids" <i>J. Org. Chem.</i> (1989) 54:3420-3422	
<i>He</i>	69	HOOKER et al. "An in vivo mutation from leucine to tryptophan at position 210 in human immunodeficiency virus type 1 reverse transcriptase contributes to high-level resistance to 3'-azido-3'-deoxythymidine" <i>J. Virol.</i> (Nov. 1996) 70(11):8010-8018	
	70 !	HOSTETLER et al. "Enhanced oral absorption and antiviral activity of 1-O-octadecyl-sn-glycero-3-phospho-acyclovir and related compounds in hepatitis B virus infection, <i>in vitro</i> " <i>Biochem. Pharmacol.</i> (1997) 53:1815-1822	
<i>He</i>	71 !	HOUZE, et al. "Detection of thymidylate synthase gene expression levels in formalin-fixed paraffin embedded tissue by semiquantitative, nonradioactive reverse transcriptase polymerase chain reaction" <i>Tumor Biol.</i> (1997) 18:53-68	

Examiner's Signature

L. E. Crane

Date Considered

03/08/2005

! Month of publication data not available on the copy supplied.

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Applicant's unique citation designation number (optional). ² Applicant is to place a check mark here if English language Translation is attached. This collection of information is required by 37 CFR 1.98. This information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 120 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

** Duplicate: see PTO-1449 for citation.

If you need assistance in completing this form, call 1-800-PTO-9199 and select option 2.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449B-PTO

INFORMATION DISCLOSURE
STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet 6 of 19

Complete if Known

Application Number	10/681,418
Filing Date	October 7, 2003
First Named Inventor	H. Michael SHEPARD
Art Unit	Lawrence E. Crane
Examiner Name	1623

Attorney Docket Number

NB 2008.01

NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher city and/or country where published	T ²
**	72	HCAIO and BARDOZ "Synthesis of 5'-thymidyl bis(1-aziridinyl)phosphinates as antineoplastic agents" <i>J. Med. Chem.</i> (19810 24:887-889	
<i>lrc</i>	73	HUDZIAK et al. "Amplified expression of the HER2/ERBB2 oncogene induces resistance to tumor necrosis factor α in NIH 3T3 cells" <i>PNAS USA</i> (July 1988) 85:5102-5106	
	74	HUSAIN et al. "Elevation of topoisomerase I messenger RNA, protein, and catalytic activity in human tumors: Demonstration of tumor-type specificity and implications for cancer chemotherapy" <i>Cancer Research</i> (Jan. 15, 1994) 54:539-546	
	75 !	JACKMAN and CALVERT "Folate-based thymidylate synthase inhibitors as anticancer drugs" <i>Ann. Oncol.</i> (1995) 6(9):871-881	
	76 !	JACKMAN et al. "Quinazoline-based thymidylate synthase inhibitors: Relationship between structural modifications and polyglutamation" <i>Anti-Cancer Drug Design</i> (1995) 10:573-589	
	77	JOHNSTON et al. "Thymidylate synthase gene and protein expression correlate and are associated with response to 5-fluorouracil in human colorectal and gastric tumors" <i>Cancer Res.</i> (April 1, 1995) 55:1407-1412	
	78	JONES and MANN "New methods of synthesis of β -aminoethylpyrazoles" <i>J. Am. Cancer Soc.</i> (Aug. 20, 1953) 75:4048-4052	
	79	KASHANI-SABET et al. "Detection of drug resistance in human tumors by <i>in vitro</i> enzymatic amplification" <i>Cancer Res.</i> (Oct. 15, 1988) 48:5775-5778	
	80	KOBAYASHI et al. "Effect of hammerhead ribozyme against human thymidylate synthase on the cytotoxicity of thymidylate synthase inhibitors" <i>Jpn. J. Cancer Res.</i> (Nov. 1995) 86:1014-1018	
<i>lrc</i>	81 !	KOMAKI et al. "Difference in thymidylate synthetase activity in involved nodes compared with primary tumor in breast cancer patients" <i>Breast Cancer Res. Tr.</i> (1995) 35(2):157-162	
**	82	KRAJEWSKA and SHUGAR "Pyrimidine ribonucleoside phosphorylase activity VS 5- and/or 6-substituted uracil and uridine analogues, including conformational aspects" <i>Biochem. Pharmacol.</i> (1982) 31(6):1097-1102	
<i>lrc</i>	83 !	KWONG et al. "Hepatitis C virus NS3/4A protease" <i>Antivir. Res.</i> (1999) 41:67-84	
<i>lrc</i>	84	LASIC "Doxorubicin in sterically stabilized liposomes" <i>Nature</i> (Apr. 11, 1996) 380:561-562	

Examiner's Signature	L. E. Crane	Date Considered	03/08/2005
----------------------	-------------	-----------------	------------

Motn of publication data not available on the copy supplied.

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Applicant's unique citation designation number (optional). ² Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.88. This information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 120 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

** INDICATE pub SEE PTO 892 for citation.

If you need assistance in completing this form, call 1-800-PTO-9199 and select option 2.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449B-PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet 7 of 19

Complete if Known

Application Number	10/681,418
Filing Date	October 7, 2003
First Named Inventor	H. Michael SHEPARD
Art Unit	Lawrence E. Crane
Examiner Name	1623

Attorney Docket Number NB 2008.01

NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher city and/or country where published	T ²
<i>Lee</i>	85 !	LEE et al. "Inhibition of mouse thymidylate synthase promoter activity by the wild-type p53 tumor suppressor protein" <i>Exp. Cell Res.</i> (1997) 234:270-276	
	86	LENZ et al. "p53 and thymidylate synthase expression in untreated stage II colon cancer: associations with recurrence, survival, and site" <i>Clinical Cancer Research</i> (May 1998) 4:1227-1234	
	87 !	LEŠ et al. "Modeling of reaction steps relevant to deoxyuridylate (dUMP) enzymatic methylation and thymidylate synthase mechanism-based inhibition" <i>Journal of Biomolecular Structure & Dynamics</i> (1998) 15(4):703-715	
	88 !	LEWIS et al. "Differential responses of human tumor cell lines to anti-p185 ^{HER2} monoclonal antibodies" <i>Cancer Immunol. Immunother.</i> (1993) 37(4):255-263	
	89	LEWIS et al. "A serum-resistant cytofection for cellular delivery of antisense oligodeoxynucleotides and plasmid DNA" <i>PNAS USA</i> . (April 1996) 93:3176-3181	
	90	LIN et al., "Rhenium188 hydroxyethylidene diphosphonate: a new generator-produced radiotherapeutic drug of potential value for the treatment of bone metastases" <i>Eur. J. Nucl. Med.</i> 24(6):590-595 (June 1997)	
	91 !	LIVAK et al. "Detection of single base differences using biotinylated nucleotides with very long linker arms" <i>Nucl. Acids Res.</i> (1992) 20(18):4831-4837	
	92	LIVINGSTON et al. "Studies with tetrahydrohomofolate and thymidylate synthetase from amethopterin-resistant mouse leukemia cells" <i>Biochemistry</i> (Aug. 1968) 7(8):2814-2818	
	93	LÖNN et al. "Higher frequency of gene amplification in breast cancer patients who received adjuvant chemotherapy" <i>Cancer</i> (Jan. 1, 1996) 77(1):107-112	
	94 !	LOOK et al. "Increased thymidine kinase and thymidylate synthase activities in human epithelial ovarian carcinoma" <i>Anticancer Res.</i> (1997) 17:2353-2356	
	95 !	LOVEJOY et al. "Animal models and the molecular pathology of cancer" <i>J. Pathol.</i> (1997) 181:130-135	
	96 !	MADEC et al. "Some characteristics of fetal and adult isoenzymes of thymidine kinase in human breast cancers" <i>Bull. Cancer</i> (1998) 75:187-194	
	97 !	MADER et al. "Resistance to 5-fluorouracil" <i>Gen. Pharma.</i> (1998) 31(5):661-666	
	98 !	MAHALINGAM et al. "Structural and kinetic analysis of drug resistant mutants of HIV-1 protease" <i>Eur. J. Biochem.</i> (1999) 263:238-245	
<i>Lee</i>	99 !	McGUIGAN et al. "Certain phosphoramidate derivatives of dideoxy uridine (ddU) are active against HIV and successfully by-pass thymidine kinase" <i>FEBS Let</i> (1994) 351:11-14	

Examiner's Signature	L. E. Crane <i>Lee Crane</i>	Date Considered	03/08/2005
----------------------	------------------------------	-----------------	------------

1. Month of publication date not available on copy supplied.

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹Applicant's unique citation designation number (optional). ²Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.88. This information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 120 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

** DUPLICATE: See PTO-892 for citation.

If you need assistance in completing this form, call 1-800-PTO-9199 and select option 2.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449B-PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet

8

of

19

Complete if Known

Application Number	10/681,418
Filing Date	October 7, 2003
First Named Inventor	H. Michael SHEPARD
Art Unit	Lawrence E. Crane
Examiner Name	1623
Attorney Docket Number	NB 2008.01

NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher city and/or country where published	T ²
JK	100	McINTEE "Probing the mechanism of action and decomposition of amino acid phosphomonoester amides of antiviral nucleoside prodrugs" <i>J. Med. Chem.</i> (1997) 40:3323-3331	
JKC	101	MEAD et al. "Pharmacologic aspects of homofolate derivatives in relation to amethopterin-resistant murine leukemia" <i>Cancer Res.</i> (Nov. 1966) 26(1):2374-2379	
JKC	102 !	MEIER et al. "ADA-bypass by lipophilic cyclosal-ddAMP pro-nucleotides a second example of the efficiency of the cyclosal-concept" <i>Bioorg. Med. Chem. Lett.</i> (1997) 7(12):1577-1582	
JKC	103 !	MEIER et al. "Cyclic saligenyl phosphotriesters of 2',3'-dideoxy-2',3'-didehydrothymidine (d4T) - a new pro-nucleotide approach" <i>Bioorg. Med. Chem. Lett.</i> (1997) 7(2):99-104	
JKC	104 !	MEIER et al. "CycloSal-pro-nucleotides: The design and biological evaluation of a new class of lipophilic nucleotide prodrugs" <i>Int'l. Antiviral News</i> (1997) 5(10):183-185	
JKC	105 !	MELTON et al. "Antibody-directed enzyme prodrug therapy (ADEPT). Review article" <i>Drugs of the Future</i> (1996) 21(2):167-181	
JKC	106	MELTON and SHERWOOD "Antibody-enzyme conjugates for cancer therapy" <i>J. Natl. Cancer Inst.</i> (Feb. 21, 1996) 88(3/4):153-165	
JKC	107	MOBASHERY and JOHNSTON "Reactions of <i>Escherichia coli</i> TEM β -lactamase with cephalothin and with C ₁₀ -dipeptidyl cephalosporin esters" <i>J. Biol. Chem.</i> (June 15, 1986) 261(17):7879-7887	
JKC	108 !	MOBASHERY et al. "Conscripting β -lactamase for use in drug delivery. Synthesis and biological activity of a cephalosporin C ₁₀ -ester of an antibiotic dipeptide" <i>J. Am. Chem. Soc.</i> (1986) 108:1685-1686	
JKC	109	MORGAN et al. "Tumor efficacy and bone marrow-sparing properties of TER286, a cytotoxin activated by glutathione S-transferase" <i>Cancer Res.</i> (June 15, 1998) 58:2568-2575	
JKC	110 !	MULDER et al. "Thymidylate synthase levels in tumor biopsies from patients with colorectal cancer" <i>Anticancer Res.</i> (1994) 14(6B):2677-2680	
JKC	111 !	MURRAY "Antibiotic resistance" <i>Adv. Internal. Med.</i> (1997) 42:339-367	
JKC	112 !	NAGATA et al. "The role of HBV DNA quantitative PCR in monitoring the response to Interferon treatment in chronic hepatitis B virus infection" <i>J. Hepatol.</i> (1999) 30:965-969	
JKC	113 !	NEGISHI et al. "Enhancement of N ⁴ -aminocytidine-induced mutagenesis by Ni ⁺⁺ ion" <i>Nucl. Acids Symposium</i> (1996) 35:137-138	
JKC	114	NICHOL and HAKALA "Comparative growth-inhibitory activity of homofolic acid against cell lines sensitive and resistant to amethopterin" <i>Biochem. Pharmacol.</i> (Oct. 1966) 15(10):1621-1623	
JKC	115 !	NICULESCU-DUVAZ and SPRINGER "Gene-directed enzyme prodrug therapy: A review of enzyme/prodrug combinations" <i>Expert Opin. Invest. Drugs</i> (1997) 6(6):685-703	

Examiner's Signature

L. E. Crane

Date Considered

03/08/2005

! Month of publication date not available on copy supplied.

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP-609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹Applicant's unique citation designation number (optional). ²Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.88. This information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 120 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing this form, call 1-800-PTO-9199 and select option 2.

10/681,418 - PTO-1449 #2

COPY FOR [] File Applicant

Substitute for form 1449B-PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet 9 of 19

Complete if Known

Application Number	10/681,418
Filing Date	October 7, 2003
First Named Inventor	H. Michael SHEPARD
Art Unit	Lawrence E. Crane
Examiner Name	1623
Attorney Docket Number	NB 2008.01

NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher city and/or country where published	T ²
<i>JLC</i>	116 !	PALMER et al. "Highly drug-resistant HIV-1 clinical isolates are cross-resistant to many antiretroviral compounds in current clinical development" <i>AIDS</i> (1999) 13(6):661-667	
	117 !	PARADISO et al. "Thymidilate synthase and p53 primary tumour expression as predictive factors for advanced colorectal cancer patients" <i>Brit. J. Cancer</i> (2000) 82(3):560-567	
	118	PATTERSON et al. "Thymidine phosphorylase moderates thymidine-dependent rescue after exposure to the thymidylate synthase inhibitor ZD1694 (tomudex) <i>in vitro</i> " <i>Cancer Res.</i> (July 1, 1998) 58:2737-2740	
	119 !	PEDERSEN-LANE et al. "High-level expression of human thymidylate synthase" <i>Protein Expression and Purification</i> (1997) 10:256-262	
	120 !	PEGRAM et al. "The effect of HER-2/neu overexpression on chemotherapeutic drug sensitivity in human breast and ovarian cancer cells" <i>Oncogene</i> (1997) 15:537-547	
	121	PESTALOZZI et al. "Prognostic importance of thymidylate synthase expression in early breast cancer" <i>J. Clin. Oncol.</i> (May 1997) 15(5):1923-1931	
	122 !	PHELPS et al. "Synthesis and biological activity of 5-fluoro-2'-deoxyuridine 5'-phosphorodiamidates" <i>J. Med. Chem.</i> (1980) 23:1229-1232	
<i>JLC</i>	123	PLUTA et al., "Synthesis and biological properties of 4-hydroxy, 4-thio-5-pyrimidine derivatives" <i>Boll. Chim. Farmaceutico</i> (Gennaio 1999) 138(1):30-33	
*8	124	ROBINS and BARR "Nucleic acid related compounds. 34. Smooth and efficient palladium-copper catalyzed coupling of terminal alkynes with 5-iodouracil nucleosides" <i>Tetrahedron Lett.</i> (1981) 22:421-424	
<i>JLC</i>	125 !	ROBINS et al. "Nucleic acid related compounds. 38. Smooth and high-yield iodination and chlorination at C-5 of uracil bases and p-tolyl-protected nucleosides" <i>Can. J. Chem.</i> (1982) 60:554-557	
**	126	ROBINS and BARR "Nucleic acid compounds. 39. Efficient conversion of 5-iodo to 5-alkynyl and derived 5-substituted uracil bases and nucleosides" <i>J. Org. Chem.</i> (1983) 48:1854-1862	
<i>JLC</i>	127 !	RODE "Specificity of thymidylate synthase inactivation by 4,5-bisubstituted dUMP analogues" <i>M. Nencki Inst. Exp. Biol., Acta Biochimica Polonica</i> (1993) 40(3):363-368	
	128 !	ROMAIN et al. "Prognostic value of cytosolic thymidine kinase activity as a marker of proliferation in breast cancer" <i>Int. J. Cancer</i> (1995) 61:7-12	
<i>JLC</i>	129 !	ROTH et al. "p53 tumor suppressor gene therapy for cancer" <i>Oncology</i> (1999) 13(10)(5):148-154	

Examiner's Signature	L. E. Crane <i>JLC</i>	Date Considered	08/08/2005
----------------------	------------------------	-----------------	------------

1. Month of publication data not available on copy supplied.

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹Applicant's unique citation designation number (optional). ²Applicant is to place a check mark here if English language Translation is attached. This collection of information is required by 37 CFR 1.98. This information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 120 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

** DUPLICATE: See PTO-892 for citation.

If you need assistance in completing this form, call 1-800-PTO-9199 and select option 2.

Substitute for form 1449B-PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet 10 of 19

Complete if Known

Application Number	10/681,418
Filing Date	October 7, 2003
First Named Inventor	H. Michael SHEPARD
Art Unit	Lawrence E. Crane
Examiner Name	1623

Attorney Docket Number

NB 2008.01

NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher city and/or country where published	T ²
	130	RUTH and BERGSTROM "6-5 substituted pyrimidine nucleosides. 1. Synthesis of C-5 allyl, propyl, and propenyl uracil and cytosine nucleosides via organopalladium intermediates" <i>J. Org. Chem.</i> (1978) 43(14):2870-2876	
<i>JLC</i>	131 !	SABOULARD et al. "Characterization of the activation pathway of phosphoramidate triester prodrugs of stavudine and zidovudine" <i>Mol. Pharmacol.</i> (1999) 56:693-704	
	132	SANTI "Perspectives on the design and biochemical pharmacology of inhibitors of thymidylate synthetase" <i>J. Med. Chem.</i> (Feb. 1980) 23(2):103-111	
	133 !	SASTRY et al. "Membrane-permeable dideoxyuridine 5'-monophosphate analogue inhibits human immunodeficiency virus infection" <i>Mol. Pharmacol.</i> (1992) 41:441-445	
	134 !	SATYAM et al. "Design, synthesis, and evaluation of latent alkylating agents activated by glutathione S-transferase" <i>J. Med. Chem.</i> (1996) 39:1736-1747	
	135 !	SHAFFER and VUITTON "Highly active antiretroviral therapy (HAART) for the treatment of infection with human immunodeficiency virus type 1" <i>Biomed. & Pharamcother.</i> (1999) 53:73-86	
	136 !	SHEPARD and LEWIS "Resistance of tumor cells to tumor necrosis factor" <i>J. Clin. Immunol.</i> (1988) 8(5):333-341	
	137	SIMON and SCHINDLER "Cell biological mechanisms of multidrug resistance in tumors" <i>PNAS USA</i> (April 1994) 91:3497-3504	
	138	SMITH et al. "Response to doxorubicin of cultured normal and cancerous human mammary epithelial cells" <i>JNCI</i> (Feb. 1985) 74(2):341-347	
	139	SMITH et al. "Preliminary correlations of clinical outcome with <i>in vitro</i> chemosensitivity of second passage human breast cancer cells" <i>Cancer Res.</i> (May 15, 1990) 50(10):2943-2948	
	140 !	SMITH et al. "Regulation and mechanisms of gene amplification" <i>Phil. Trans. R. Soc. Lond. B.</i> (1995) 347:49-56	
	141 !	STÜHLINGER et al. "Clinical therapy and HER-2 oncogene amplification in breast cancer: Chemo vs radiotherapy" <i>J. Steroid Biochem. Molec. Biol.</i> (1994) 49(1):39-42	
	142	SUGARMAN et al. "Recombinant human tumor necrosis factor- α : Effects on proliferation of normal and transformed cells <i>in vitro</i> " <i>Science</i> (Nov. 22, 1985) 230(4728):943-945	
	143 !	SUKI et al. "Risk classification for large cell lymphoma using lactate dehydrogenase, beta-2 microglobulin, and thymidine kinase" <i>Leukemia and Lymphoma</i> (1995) 18:87-92	
<i>JLC</i>	144	TANNOCK "Treatment of cancer with radiation and drugs" <i>J. Clin. Oncol.</i> (Dec. 1996) 14(12):3156-3174	

Examiner's Signature

L. E. Crane

Date Considered

03/08/2005

! Month of publication data not available on copy supplied.

* EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Applicant's unique citation designation number (optional). ² Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.98. This information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 120 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

** DUPLICATE: See PTO-892 for citation.

If you need assistance in completing this form, call 1-800-PTO-9199 and select option 2.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

¹ Substitute for form 1449B-PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet 11 of 19

Complete if Known

Application Number	10/681,418
Filing Date	October 7, 2003
First Named Inventor	H. Michael SHEPARD
Art Unit	Lawrence E. Crane
Examiner Name	1623

Attorney Docket Number NB 2008.01

NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher city and/or country where published	T ²
	145 !	TEH et al. "Tumor suppressor genes (TSG)" <i>Anticancer Research</i> (1999) 19:4715-4728	
	146 !	TOLSTIKOV et al. "Synthesis and DNA duplex stabilities of oligonucleotides containing C-5-(3-methoxypropynyl)-2'-deoxyuridine residues" <i>Nucleos. Nucleot.</i> (1997) 16(3):215-225	
	147	TOUROUTOGLOU and PAZDAR "Thymidylate synthase inhibitors" <i>Clin. Cancer Res.</i> (Feb. 1996) 2(2):227-243	
	148 !	TROUTNER "Chemical and physical properties of radionuclides" <i>Nucl. Med. Biol.</i> (1987) 14(3):171-176	
	149 !	TURNER and SUMMERS "Structural biology of HIV" <i>J. Mol. Biol.</i> (1999) 285:1-32	
	150 !	VALETTE et al. "Decomposition pathways and <i>in vitro</i> HIV inhibitory effects of isoddA pronucleotides: Toward a rational approach for intracellular delivery of nucleoside 5'-monophosphates" <i>J. Med. Chem.</i> (1996) 39:1981-1990	
	151	van LAAR "Therapeutic efficacy of fluoropyrimidines depends on the duration of thymidylate synthase inhibition in the murine colon 26-B carcinoma tumor model" <i>Clin. Cancer Res.</i> (Aug. 1996) 2(8):1327-1333	
	152	van TRIEST et al. "Thymidylate synthase level as the main predictive parameter for sensitivity to 5-fluorouracil, but not for folate-based thymidylate synthase inhibitors, in 13 nonselected colon cancer cell lines" <i>Clin. Cancer Res.</i> (Mar. 1999) 5(3):643-654	
	153	WAHBA and FRIEDKIN "Direct spectrophotometric evidence for the oxidation of tetrahydrofolate during the enzymatic synthesis of thymidylate" <i>J. Biol. Chem.</i> (Mar. 1961) 236(3):C11-C12	
	154 !	WALLIS et al. "Synthesis and anti-HIV activity of C4-modified pyrimidine nucleosides" <i>Il Farmaco</i> (1999) 54:83-89	
	155 !	WANG "Protease Inhibitors as potential anti-viral agents for the treatment of picornaviral infections" <i>Prog. Drug Res.</i> (1999) 52:197-219	
	156	WATAYA et al. "trans-5-(3,3,3-trifluoro-1-propenyl)-2'-deoxyuridylate: A mechanism-based inhibitor of thymidylate synthetase" <i>J. Med. Chem.</i> (Apr. 1979) 22(4):339-340	
	157	WATAYA et al. "Interaction of thymidylate synthetase with 5-nitro-2'-deoxyuridylate" <i>J. Biol. Chem.</i> (June 25, 1980) 255(12):5538-5544	
	158 !	WETTERGREN et al. "Drug-specific rearrangements of chromosome 12 in hydroxyurea-resistant mouse SEWA cells: Support for chromosomal breakage model of gene amplification" <i>Somat. Cell Molec. Gen.</i> (1994) 20(4):267-285	

Examiner's Signature L. E. Crane Date Considered 03/08/2005

! Month of publication data not available on the copy supplied.

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Applicant's unique citation designation number (optional). ² Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.98. This information is required to obtain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 120 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing this form, call 1-800-PTO-9199 and select option 2.

10/681,418 PTO-1449 #2

COPY FOR [] File [] *Applicant*

Substitute for form 1449B-PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet

12

of

19

Complete if Known

Application Number	10/681,418
Filing Date	October 7, 2003
First Named Inventor	H. Michael SHEPARD
Art Unit	Lawrence E. Crane
Examiner Name	1623
Attorney Docket Number	NB 2008.01

NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher city and/or country where published	T ²
<i>Mc</i>	159 !	WHALEN and BOYER "Human glutathione S-transferases" <i>Seminars in Liver Disease</i> (1998) 18(4):345-358	
	160 !	WILDNER et al. "Enzyme prodrug gene therapy: Synergistic use of the herpes simplex virus-cellular thymidine kinase/ganciclovir system and thymidylate synthase inhibitors for the treatment of colon cancer" <i>Cancer Res.</i> (Oct. 15, 1999) 59(20):5233-5238	
	161	WOLFE et al. "Antibody-directed enzyme prodrug therapy with the T268G mutant of human carboxypeptidase A1: in vitro and in vivo studies with prodrugs of methotrexate and the thymidylate synthase inhibitors GW1031 and GW1843" <i>Bioconjugate Chem.</i> (1999) 10(1):38-48	
	162	YEN et al. "Characterization of a hydroxyurea-resistant human KB cell line with supersensitivity to 6-thioguanine" <i>Cancer Res.</i> (July 15, 1994) 54:3686-3691	
<i>Mc</i>	163	ZEID et al. "Synthesis of new thiolated acyclonucleosides with potential anti-HBV activity" <i>Nucleos. Nucleot.</i> (1999) 18(1):95-111	
	164 !	ANDERSEN et al. "Detection of C-ERBB-2 related protein in sera from breast cancer patients" <i>Acta Oncol.</i> (1995) 34(4):499-504	
	165 !	AYISI et al. "Comparison of the antiviral effects of 5-methoxymethyldeoxyuridine-5'-monophosphate with adenine arabinoside-5'-monophosphate" <i>Antivir. Res.</i> (1983) 3:161-174	
	166 !	BALZARINI et al. "Thymidylate synthase is the principal target enzyme for the cytostatic activity of (E)-5-(2-bromovinyl)-2'-deoxyuridine against murine mammary carcinoma (FM3A) cells transformed with the herpes simplex virus type 1 or type 2 thymidine kinase gene" <i>Mol. Pharmacol.</i> (1987) 32:410-416	
	167	BALZARINI et al. "Differential mechanism of cytostatic effect of (E)-5-(2-bromovinyl)-2'-deoxyuridine, 9-(1,3-dihydroxy-2-propoxymethyl)guanine, and other antiherpetic drugs on tumor cells transfected by the thymidine kinase gene of herpes simplex virus type 1 or type 2" <i>J. Biol. Chem.</i> (1993) 268(9):6332-6337 (March 25, 1993)	
	168 !	BALZARINI et al. "Anti-HIV and anti-HBV activity and resistance profile of 2',3'-dideoxy-3'-thiacytidine (3TC) and its arylphosphoramidate derivative CF 1109" <i>Biochem. Biophys. Res. Co.</i> (1996) 225:363-369	
<i>Mc</i>	169 !	BALZARINI et al. "Conversion of 2',3'-dideoxyadenosine (ddA) and 2',3'-didehydro-2',3'-dideoxyadenosine (d4A) to their corresponding arylxylophosphoramidate derivatives markedly potentiates their activity against human immunodeficiency virus and hepatitis B virus" <i>FEBS Lett.</i> (1997) 410:324-328	
**	170	BARR "Inhibition of thymidylate synthetase by 5-alkynyl-2'-deoxyuridylates" <i>J. Med. Chem.</i> (1981) 24(12):1385-1388	

Examiner's Signature

L. E. Crane

Date Considered

03/08/2005

Month of publication data not available on copy supplied.

* EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Applicant's unique citation designation number (optional). ² Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.98. This information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 120 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

** Duplicate: see pto-892 for citation.

If you need assistance in completing this form, call 1-800-PTO-9199 and select option 2.

Complete if Known

Substitute for form 1449B-PTO

INFORMATION DISCLOSURE
STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet 13 of 19

Application Number	10/681,418
Filing Date	October 7, 2003
First Named Inventor	H. Michael SHEPARD
Art Unit	Lawrence E. Crane
Examiner Name	1623
Attorney Docket Number	NB 2008.01

NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher city and/or country where published	T ²
<i>HC</i>	171 !	BARR et al. "Thymidylate synthetase-catalyzed conversions of <i>E</i> -5-(2-bromovinyl)-2'-deoxyuridylate" <i>J. Biol. Chem.</i> (1983) 258(22):13627-13631	
<i>HC</i>	172 !	BERGSTROM et al. "C-5-substituted pyrimidine nucleosides. 3. Reaction of allylic chlorides, alcohols, and acetates with pyrimidine nucleoside derived organopalladium intermediates" <i>J. Org. Chem.</i> (1981) 46(7):1432-1441	
**	173	BERKOW et al. (eds), <i>The Merck Manual of Diagnosis and Therapy</i> , 16th Edition, Merck & Co., Rahway, NJ, (May 1992) only page 1278 supplied	
<i>HC</i>	174 !	BOSSLET et al. "A novel one-step tumor-selective prodrug activation system" <i>Tumor Targeting</i> (1995) 1:45-50	
	175	BOSSLET et al. "Elucidation of the mechanism enabling tumor selective prodrug monotherapy" <i>Cancer Res.</i> (Mar 15, 1998) 58:1195-1201	
	176	BRISON "Gene amplification and tumor progression" <i>Biochim. Biophys. Acta</i> (1993) 1155:25-41	
	177	CARL et al. "Protease-activated 'prodrugs' for cancer chemotherapy" <i>PNAS USA</i> (April 1980) 77(4):2224-2228	
	178 !	CAVA and LEVINSON "Thionation reactions of Lawesson's reagents" <i>Tetrahedron</i> (1985) 41(22):5061-5087	
	179 !	CHAKRAVARTY et al. "Plasmin-activated prodrugs for cancer chemotherapy. 2. Synthesis and biological activity of peptidyl derivatives of doxorubicin" <i>J. Med. Chem.</i> (1983) 26(5):638-644	
	180 !	COLACINO "Mechanisms for the anti-hepatitis B virus activity and mitochondrial toxicity of fialuridine (FIAU)" <i>Antivir. Res.</i> (1996) 29:125-139	
	181	COLLINS et al. "Suicide prodrugs activated by Thymidylate synthase: Rationale for treatment and noninvasive imaging of tumors with deoxyuridine analogues" <i>Clin. Cancer Res.</i> (August 1999) 5:1976-1981	
<i>HC</i>	182 !	CONNORS "Prodrugs in cancer chemotherapy" <i>Xenobiotica</i> (1986) 16(10/11):975-988	
<i>HC</i>	183 !	CONNORS "Is there a future for cancer chemotherapy?" <i>Ann. Oncol.</i> (1996) 7:445-452	
**	184	DAGLE et al. "Targeted degradation of mRNA in Xenopus oocytes and embryos directed by modified oligonucleotides: Studies of An2 and Cyclin in embryogenesis" <i>Nucleic Acids Res.</i> (Aug. 25, 1990) 18(16):4751-4757	
<i>HC</i>	185 !	DAVISSON et al. "Expression of human thymidylate synthase in <i>Escherichia coli</i> " <i>J. Biol. Chem.</i> (1989) 264(16):9145-9148	

Examiner's Signature	L. E. Crane <i>L. Crane</i>	Date Considered	03/08/2005
----------------------	-----------------------------	-----------------	------------

! Month of publication date not available on the copy supplied.

* EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Applicant's unique citation designation number (optional). ² Applicant is to place a check mark here if English language Translation is attached.
 This collection of information is required by 37 CFR 1.98. This information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 120 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

** DUPLICATE: Pto-892 for citation.

If you need assistance in completing this form, call 1-800-PTO-9199 and select option 2.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449B-PTO

INFORMATION DISCLOSURE
STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet

14

of

19

Complete if Known

Application Number	10/681,418
Filing Date	October 7, 2003
First Named Inventor	H. Michael SHEPARD
Art Unit	Lawrence E. Crane
Examiner Name	1623
Attorney Docket Number	NB 2008.01

NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher city and/or country where published	T ²
	186	DAVISSON et al. "Expression of human thymidylate synthase in <i>Escherichia coli</i> . (Additions and corrections)" <i>J. Biol. Chem.</i> (Dec. 2, 1994) 269(48):30740	
	187	DeCLERCQ "In search of a selective antiviral chemotherapy" <i>Clin. Microbiol. Rev.</i> (Oct. 1997) 10(4):674-693	
	188 !	DRAKE et al. "Resistance to Tomudex (ZD1694): Multifactorial in Human Breast and Colon Carcinoma Cell Lines" <i>Biochem. Pharmacol.</i> (1996) 51(10):1349-1355	
	189 !	ECCLES et al. "Significance of the c-erbB family of receptor tyrosine kinases in metastatic cancer and their potential as targets for immunotherapy" <i>Invasion Metastasis</i> (1994-95) 14(1-6):337-348	
	190 !	EISENBRAND et al. "An approach towards more selective anticancer agents" <i>J. Synthetic Organic Chem.</i> (1996) 10:1246-1258	
**	191	EVARD et al. "An in vitro nucleoside analog screening method for cancer gene therapy" <i>Cell Biol. Toxicol.</i> (1996) 12:345-350	
	192 !	EVARD et al. "An in vitro nucleoside analog screening method for cancer gene therapy" <i>Chem. Abstracts</i> (1996) 126:Abstract No. 26514	
	193	FELIP et al. "Overexpression of c-erbB-2 in epithelial ovarian cancer" <i>Cancer</i> (Apr. 15, 1995) 75(8):2147-2152	
	194 !	FINCH "Radiation Injury" In: <i>Harrison's Principles of Internal Medicine</i> , 12th Edition, McGraw-Hill, Inc., New York, NY (1991) 2204-2208	
	195 !	FINER-MOORE et al. "Refined structures of substrate-bound and phosphate-bound thymidylate synthase from <i>Lactobacillus casei</i> " <i>J. Mol. Biol.</i> (1993) 232:1101-1116	
	196 !	FINER-MOORE et al. "Crystal structure of thymidylate synthase from T4 phage: Component of a deoxynucleoside triphosphate-synthesizing complex" <i>Biochemistry</i> (1994) 33:15459-15468	
**	197	FIRESTONE et al. "A comparison of the effects of antitumor agents upon normal human epidermal keratinocytes and human squamous cell carcinoma" <i>J. Invest. Dermatol.</i> (May 1990) 94(5):657-661	
	198 !	FIRESTONE et al. "A comparison of the effects of antitumor agents upon normal human epidermal keratinocytes and human squamous cell carcinoma" <i>Chem Abstracts</i> (1990) 113:Abstract No. 254	
	199 !	GARRETT et al. "Thymidylate synthetase. Catalysis of dehalogenation of 5-bromo-and 5-iodo-2'-deoxyuridylate" <i>Biochemistry</i> (1979) 18(13):2798-2804	
	200 !	GOLDBERG et al. "Novel cell imaging techniques show induction of apoptosis and proliferation in mesothelial cells by asbestos" <i>Am. J. Respir. Cell Mol. Biol.</i> (1997) 17:265-271	

Examiner's Signature	L. E. Crane	Date Considered	03/08/2005
----------------------	-------------	-----------------	------------

! Month of publication data not available on the copy supplied.

* EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Applicant's unique citation designation number (optional). ² Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.98. This information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 120 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

** Duplicate: See PTO-892 for citation.

If you need assistance in completing this form, call 1-800-PTO-9199 and select option 2.

Substitute for form 1449B-PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet 15 of 19

Complete if Known

Application Number	10/681,418
Filing Date	October 7, 2003
First Named Inventor	H. Michael SHEPARD
Art Unit	Lawrence E. Crane
Examiner Name	1623

Attorney Docket Number NB 2008.01

NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher city and/or country where published	T ²
<i>He</i>	201	GROS et al. "Isolation and expression of a complementary DNA that confers multidrug resistance" <i>Nature</i> (Oct. 1986) 323:728-731	
	202	GROS et al. "Mammalian multidrug resistance gene: Complete cDNA sequence indicates strong homology to bacterial transport proteins" <i>Cell</i> (Nov. 7, 1986) 47:371-380	
	203	GROS et al. "Isolation and characterization of DNA sequences amplified in multidrug-resistant hamster cells" <i>PNAS USA</i> (Jan. 1986) 83:337-341	
<i>He</i>	204 !	GUDKOV et al. "Cloning and characterization of DNA sequences amplified in multidrug-resistant djungarian hamster and mouse cells" <i>Somat. Cell Mol. Genet.</i> (1987) 13(6):609-619	
<i>xx</i>	205	HAKIMELAH et al. "Design, synthesis and structure-activity relationship of novel dinucleotide analogs as agents against herpes and human immunodeficiency viruses" <i>J. Med. Chem.</i> (Nov. 10, 1995) 38(23):4648-4659	
<i>He</i>	206	HARDY et al. "Atomic structure of thymidylate synthase: Target for rational drug design" <i>Science</i> (Jan. 23, 1987) 235:448-455	
	207 !	HARRIS et al. "Adenovirus-mediated p53 gene transfer inhibits growth of human tumor cells expressing mutant p53 protein" <i>Cancer Gene Ther.</i> (1996) 3(2):121-130	
	208 !	HASHIMOTO et al. "Simple separation of tritiated water and [³ H]deoxyuridine from [5- ³ H]deoxyuridine 5'-monophosphate in the thymidylate synthase assay" <i>Anal. Biochem.</i> (1987) 167:340-346	
	209 !	HENGSTSCHLÄGER et al. "The role of p16 in the E2F-dependent thymidine kinase regulation" <i>Oncogene</i> (1996) 12:1635-1643	
	210 !	HOLÝ et al. "Structure-Antiviral Activity Relationship in the Series of Pyrimidine and Purine N-[2-(2-Phosphonomethoxy)ethyl] Nucleotide Analogues. 1. Derivatives Substituted at the Carbon Atoms of the Base" <i>J. Med. Chem.</i> (1999) 42(12):2064-2086	
	211	HORIKOSHI et al. "Quantitation of thymidylate synthase, dihydrofolate reductase, and DT-diaphorase gene expression in human tumors using the polymerase chain reaction" <i>Cancer Res.</i> (Jan. 1, 1992) 52:108-116	
	212 !	HORN et al. "Fialuridine is phosphorylated and inhibits DNA synthesis in isolated rat hepatic mitochondria" <i>Antivir. Res.</i> (1997) 34:71-74	
	213 !	HUANG and SANTI "Active site general catalysts are not necessary for some proton transfer reactions of thymidylate synthase" <i>Biochemistry</i> (1997) 36:1869-1873	
<i>He</i>	214 !	HUDZIAK et al. "Selection for transformation and met protooncogene amplification in NIH 3T3 fibroblasts using tumor necrosis factor α " <i>Cell Growth & Differentiation</i> (1990) 1:129-134	

Examiner's Signature	L. E. Crane <i>He</i>	Date Considered	03/08/2005
----------------------	-----------------------	-----------------	------------

! Month of publication date not available on the copy supplied.

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Applicant's unique citation designation number (optional). ² Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.98. This information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 120 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

** DUPLICATE! See PTO-892 for citation.

If you need assistance in completing this form, call 1-800-PTO-9199 and select option 2.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449B-PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet 16 of 19

Complete if Known

Application Number	10/681,418
Filing Date	October 7, 2003
First Named Inventor	H. Michael SHEPARD
Art Unit	Lawrence E. Crane
Examiner Name	1623
Attorney Docket Number	NB 2008.01

NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher city and/or country where published	T ²
<i>REC</i>	215 !	HUSAK et al. "Pseudotumour of the tongue caused by herpes simplex virus type 2 in an HIV-1 infected immunosuppressed patient" <i>Brit. J. Dermatol.</i> (1998) 139:118-121	
	216	IMAI et al. "Studies on phosphorylation. IV. Selective phosphorylation of the primary hydroxyl group in nucleosides" <i>J. Org. Chem.</i> (June 1969) 34(6):1547-1550	
	217	JOHNSTON et al. "Production and characterization of monoclonal antibodies that localize human thymidylate synthase in the cytoplasm of human cells and tissue" <i>Cancer Res.</i> (Dec. 15, 1991) 51:6668-6676 <i>et al.</i>	
	218	JOHNSTON <i>The role of thymidylate synthase expression in prognosis and outcome of adjuvant chemotherapy in patients with rectal cancer</i> <i>J. Clin. Oncol.</i> (Dec. 1994) 12(12):2640-2647	
	219 !	KAMB "Cyclin-dependent kinase inhibitors and human cancer" <i>Curr. Top. Microbiol. Immunol.</i> (1998) 227:139-148	
	220	KATKI et al. "Prodrugs activated by thymidylate synthase: Treatment of tumors with deoxyuridine analogs" <i>Proc. Amer. Assoc. Cancer Res.</i> (March 1998) 39:Abstract No. 1275	
	221 !	KLECKER et al. "Toxicity, metabolism, DNA incorporation with lack of repair, and lactate production for 1-(2'-fluoro-2'-deoxy-β-D-arabinofuranosyl)-5-iodouracil in U-937 and MOLT-4 cells" <i>Mol. Pharmacol.</i> (1994) 46:1204-1209	
	222	KNIGHTON et al. "Structure of and kinetic channelling in bifunctional dihydrofolate reductase-thymidylate synthase" <i>Nature Struct. Biol.</i> (March 1994) 1(3):186-194	
	223 !	KODAMA et al. "Evaluation of antiherpetic compounds using a gastric cancer cell line: Pronounced activity of BVDU against herpes simplex virus replication" <i>Microbiol. Immunol.</i> (1996) 40(5):359-363	
	224	KUMAR et al. "Synthesis and biological evaluation of some cyclic phosphoramidate nucleoside derivatives" <i>J. Med. Chem.</i> (Sept. 1990) 33(9):2368-2374	
	225 !	KUNDU et al. "Synthesis and biological activities of [E]-5-(2-acetylvinyl) uracils" <i>Eur. J. Med. Chem.</i> (1993) 28:473-479	
	226	KUROBOSHI and HIYAMA "A facile synthesis of difluoromethylene compounds by oxidative fluorodesulfurization of dithioacetals using tetrabutylammonium dihydrogenfluoride and N-halo compounds" <i>SYNLETT</i> (Dec. 1991) pp. 909-910	
	227	KUROBOSHI and HIYAMA "A facile synthesis of α,α-difluoroalkyl ethers and carbonyl fluoride acetals by oxidative desulfurization-fluorination" <i>SYNLETT</i> (April 1994) pp. 251-252	
	228 !	LAM "Application of combinatorial library methods in cancer research and drug discovery" <i>Anti-Cancer Drug Design</i> (1997) 12:145-167	
<i>REC</i>	229 !	LARSSON et al. "Thymidylate synthase in advanced gastrointestinal and breast cancers" <i>Acta Oncologica</i> (1996) 35(4):469-472	

Examiner's Signature	L. E. Crane <i>REC</i>	Date Considered	03/08/2005
----------------------	------------------------	-----------------	------------

! Month of publication date not provided in the copy supplied.

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹Applicant's unique citation designation number (optional). ²Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.98. This information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 120 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing this form, call 1-800-PTO-9199 and select option 2.

10/681,418 - PTO-1449 #2

COPY FOR [] File [] Applicant

Substitute for form 1449B-PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet 17 of 19

Complete if Known

Application Number	10/681,418
Filing Date	October 7, 2003
First Named Inventor	H. Michael SHEPARD
Art Unit	Lawrence E. Crane
Examiner Name	1623

Attorney Docket Number

NB 2008.01

NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher city and/or country where published	T ²
<i>ME</i>	230	LI et al. "Lack of functional retinoblastoma protein mediates increased resistance to antimetabolites in human sarcoma cell lines" <i>PNAS USA</i> (Oct. 1995) 92:10436-10440	
	231	LIVINGSTONE et al. "Altered cell cycle arrest and gene amplification potential accompany loss of wild-type p53" <i>Cell</i> (Sept. 18, 1992) 70:923-935	
	232 !	MASTERS and ALTARDI "The nucleotide sequence of the cDNA coding for the human dihydrofolic acid reductase" <i>Gene</i> (1983) 21:59-63	
	233 !	McGUIGAN "Aryl phosphate derivatives of AZT retain activity against HIV1 in cell lines which are resistant to the action of AZT" <i>Antivir. Res.</i> (1992) 17:311-321	
	234 !	McGUIGAN "Intracellular delivery of bioactive AZT nucleotides by aryl phosphate derivatives of AZT" <i>J. Med. Chem.</i> (1993) 36:1048-1052	
	235 !	McGUIGAN "Aryl phosphoramidate derivatives of d4T have improved anti-HIV efficacy in tissue culture and may act by the generation of a novel intracellular metabolite" <i>J. Med. Chem.</i> (1996) 39:1748-1753	
	236 !	McGUIGAN et al. "Synthesis and evaluation of some masked phosphate esters of the anti-herpetic drug 882C (netivudine) as potential antiviral agents" <i>Antivir. Chem. Chemoth.</i> (1998) 9:187-197	
	237 !	MCKAY et al. "Broad spectrum aminoglycoside phosphotransferase type III from <i>Enterococcus</i> : Overexpression, purification, and substrate specificity" <i>Biochemistry</i> (1994) 33:6936-6944	
	238 !	MEDEN et al. "Elevated serum levels of a c-erbB-2 oncogene product in ovarian cancer patients and in pregnancy" <i>J. Cancer Res. Clin. Oncol.</i> (1994) 120:378-381	
	239 !	MONTFORT and WEICHSEL "Thymidylate synthase: Structure, inhibition, and strained conformations during catalysis" <i>Pharmacol. Ther.</i> (1997) 76(1-3):29-43	
<i>ME</i>	240 !	MONTGOMERY et al., "Phosphonate analogue of 2'-deoxy-5-fluorouridylic acid" <i>J. Med. Chem.</i> (1979) 22(1):109-111	
**	241	MORRISON & BOYD (eds) <i>Organic Chemistry</i> , Allyn & Bacon, Inc., Boston, MA, (1973) only pages 1170-1180 supplied	
<i>ME</i>	242 !	MURAKAMI and SEKIYA "Accumulation of genetic alterations and their significance in each primary human cancer and cell line" <i>Mutat. Res.</i> (1998) 400(1-2):421-437	
**	243	NAESENS et al. "Anti-HIV activity and metabolism of phosphoramidate derivatives of D4T-MP with Variations in the amino acid moiety" Poster Session 1, <u>The Tenth International Conference on Antiviral Research</u> , Hotel Nikko, Atlanta, GA April 6-11, 1997; published in <i>Antivir. Research</i> (April 1997) 34(2):A54 (Abstract 40)	
<i>ME</i>	244 !	NAKANO et al., "Critical role of phenylalanine 34 of human dihydrofolate reductase in substrate and inhibitor binding and in catalysis" <i>Biochemistry</i> (1994) 33:9945-9952	

Examiner's Signature	L. E. Crane	Date Considered	03/08/2005
----------------------	-------------	-----------------	------------

! Month of publication data not available in the copy supplied.

* EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Applicant's unique citation designation number (optional). ² Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.98. This information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 120 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing this form, call 1-800-PTO-9199 and select option 2.

Substitute for form 1449B-PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet 18 of 19

Complete if Known

Application Number	10/681,418
Filing Date	October 7, 2003
First Named Inventor	H. Michael SHEPARD
Art Unit	Lawrence E. Crane
Examiner Name	1623

Attorney Docket Number NB 2008.01

NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher city and/or country where published	T ²
<i>me</i>	245 !	NOOTER and STOTER "Molecular mechanisms of multidrug resistance in cancer chemotherapy" <i>Path. Res. Pract.</i> (1996) 192:768-780	
<i>me</i>	246 !	OSAKI et al. "5-fluorouracil (5-FU) induced apoptosis in gastric cancer cell lines: Role of the p53 gene" <i>Apoptosis</i> (1997) 2:221-226	
<i>me</i>	247 !	OSHIRO et al. "Genotoxic properties of (E)-5-(2-bromovinyl)-2'-deoxyuridine (BVDU)" <i>Fundam. Appl. Toxicol.</i> (1992) 18:491-498	
NS	248	PARDO et al. "The incorporation of deoxyuridine monophosphate in DNA increases the sister-chromatid exchange yield" <i>Exp Cell Res.</i> (1987) 168:507-517	
<i>me</i>	249	PARK et al. "Chemotherapy efficacy of E-5-(2-bromovinyl)-2'-deoxyuridine for orofacial infection with herpes simplex virus type 1 in mice" <i>J. Infectious Diseases</i> (June 1982) 145(6):909-913	
<i>me</i>	250 !	PERRY et al. "Plastic adaptation toward mutations in proteins: Structural comparison of thymidylate synthases" <i>Proteins</i> (1990) 8:315-333	
<i>me</i>	251 !	PETERS et al. "Thymidylate synthase and drug resistance" <i>Eur. J. Can.</i> (1995) 31A(7/8):1299-1305	
NS	252	PUPA et al. "The extracellular domain of the erbB-2 oncogene is released from tumor cells by proteolytic cleavage" <i>Oncogene</i> (1993) 8:2917-2923	
<i>me</i>	253	ROBERTS "An isotopic assay for thymidylate synthetase" <i>Biochemistry</i> (Nov. 1966) 5(11):3546-3548	
	254	ROGULSKI et al. "Glioma cells transduced with an <i>Escherichia coli</i> CD/HSV-1 TK fusion gene exhibit enhanced metabolic suicide and radiosensitivity" <i>Hum. Gene Ther.</i> (Jan. 1, 1997) 8:73-85	
	255	RONINSON et al. "Amplification of specific DNA sequences correlates with multi-drug resistance in Chinese hamster cells" <i>Nature</i> (June 14, 1984) 309:626-628	
	256	SAUTER et al. "Heterogeneity of erbB-2 gene amplification in bladder cancer" <i>Cancer Res.</i> (May 15, 1993) 53:2199-2203	
	257 !	SCHIFFER et al. "Crystal structure of human thymidylate synthase: A structural mechanism for guiding substrates into the active site" <i>Biochemistry</i> (1995) 34:16279-16287	
	258	SCHIMKE "Gene amplification in cultured cells" <i>J. Biol. Chem.</i> (May 5, 1988) 263(13):5989-5992	
	259 !	SEGOVIA "Leishmania gene amplification: A mechanism of drug resistance" <i>Ann. Trop. Med. Parasit.</i> (1994) 88(2):123-130	
	260 !	SINGH et al. "Studies on the preparation and isomeric composition of ¹⁸⁶ Re- and ¹⁸⁸ Re-pentavalent rhenium dimercaptosuccinic acid complex" <i>Nucl. Med. Commun.</i> (1993) 14:197-203	
	261	SLAMON et al. "Human breast cancer: Correlation of relapse and survival with amplification of the HER-2/neu oncogene" <i>Science</i> (Jan. 9, 1987) 235:177-182	
<i>me</i>	262	SLAMON et al. "Studies of the HER-2/neu proto-oncogene in human breast and ovarian cancer" <i>Science</i> (May 12, 1989) 244:707-712	

Examiner's Signature	L. E. Crane <i>L. E. Crane</i>	Date Considered	03/08/2005
----------------------	--------------------------------	-----------------	------------

1. Month of publication data not available in the copy supplied.

EXAMINER: Initial reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹Applicant's unique citation designation number (optional). ²Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.98. This information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 120 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

no copy found in electronic files (scanned).

NS - Not submitted: If you need assistance in completing this form, call 1-800-PTO-9199 and select option 2.

Substitute for form 1449B-PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet 19 of 19

Complete if Known

Application Number	10/681,418
Filing Date	October 7, 2003
First Named Inventor	H. Michael SHEPARD
Art Unit	Lawrence E. Crane
Examiner Name	1623

Attorney Docket Number

NB 2008.01

NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher city and/or country where published	T ²
<i>lmc</i>	263 !	SNYDMAN et al. "Analysis of trends in antimicrobial resistance patterns among clinical isolates of <i>Bacteroides fragilis</i> group species from 1990 to 1994" <i>Clin. Infect. Dis.</i> (1996) 23(Suppl. 1):S54-S65	
<i>lmc</i>	264 !	STASCHKE et al. "The in vitro anti-hepatitis B virus activity of FIAU [1-(2'-deoxy-2'-fluoro-1-β-D-arabinofuranosyl-5-iodo)uracil] is selective, reversible, and determined, at least in part, by the host cell" <i>Antiviral Res.</i> (1994) 23:45-61	
<i>lmc</i>	265 !	STOUT et al. "Structure-based design of inhibitors specific for bacterial thymidylate synthase" <i>Biochemistry</i> (1999) 38:1607-1617	
<i>lmc</i>	266	SUKUMAR and BARBACID "Specific patterns of oncogene activation in transplacentally induced tumors" <i>PNAS USA</i> (Jan. 1990) 87:718-722	
<i>lmc</i>	267 !	TAKEISHI et al. "Nucleotide sequence of a functional cDNA for human thymidylate synthase" <i>Nucl. Acid Res.</i> (1985) 13(6):2035-2043	
<i>lmc</i>	268	TENNANT et al. "Antiviral activity and toxicity of fialuridine in the woodchuck model of hepatitis B virus infection" <i>Hepatology</i> (July 1998) 28(1):179-191	
<i>lmc</i>	269	TOWNSEND (ed.), <i>Chemistry of Nucleosides and Nucleotides</i> , Vol. 3, Plenum Press, New York, NY (1974) only Table of Contents, Bibliography, pages 529-535 and Index pp. 537-552 supplied	
<i>lmc</i>	270	UBEDA and HABENER "The large subunit of the DNA replication complex C (DSEB/RF-C140) cleaved and inactivated by Caspase-3 (CPP32/YAMA) during fas-induced apoptosis" <i>J. Biol. Chem.</i> (Aug. 1, 1997) 272(31):19562-19568	
<i>lmc</i>	271 !	van de VIJVER et al. "Amplification of the <i>neu</i> (c-erbB-2) oncogene in human mammary tumors is relatively frequent and is often accompanied by amplification of the linked c-erbA oncogene" <i>Mol. Cell. Biol.</i> (May 1987) 7(5):2019-2023	
<i>lmc</i>	272	VOLM et al. "Relationship of inherent resistance to doxorubicin, proliferative activity and expression of P-glycoprotein 170, and glutathione S-transferase- π in human lung tumors" <i>Cancer</i> (Aug. 15, 1992) 70(4):764-769	
<i>lmc</i>	273	WANG et al. "Identification and characterization of Ich-3, a member of the interleukin-1 β converting enzyme (ICE)/Ced-3 family and an upstream regulator of ICE" <i>J. Biol. Chem.</i> (Aug. 23, 1996) 271(34):20580-20587	
<i>lmc</i>	274	YIN et al. "Wild-type p53 restores cell cycle control and inhibits gene amplification in cells with mutant p53 alleles" <i>Cell</i> (Sept. 18, 1992) 70:937-948	
<i>lmc</i>	275	ZHOU et al. "Target protease specificity of the viral serpin CrmA" <i>J. Biol. Chem.</i> (Mar. 21, 1997) 272(12):7797-7800	
<i>lmc</i>	276	<i>The American Heritage College Dictionary</i> , Third Edition, Houghton Mifflin Co., New York, NY (1997) only page 668 supplied	

Examiner's Signature	L. E. Crane <i>lmc</i>	Date Considered	03/08/2005
----------------------	------------------------	-----------------	------------

! Month of publication data/not available in the copy supplied.

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Applicant's unique citation designation number (optional). ² Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.98. This information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 120 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

** DUPLICATE: See PTO-892 for citation.

If you need assistance in completing this form, call 1-800-PTO-9199 and select option 2.